



**Armed Forces College of  
Medicine  
AFCM**



# Diuretics (1)

**By**

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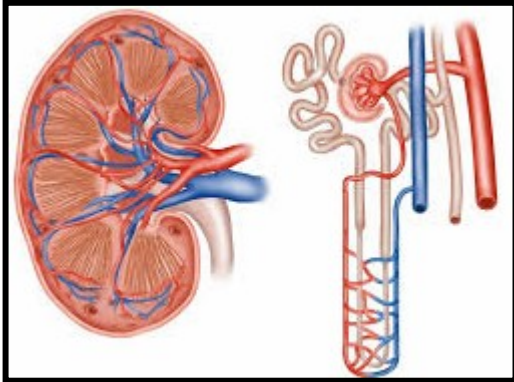
**Dermatology and Andrology  
Specialist /ASU**

## **INTENDED LEARNING OBJECTIVES (ILO)**



**By the end of this lecture the student will be able to:**

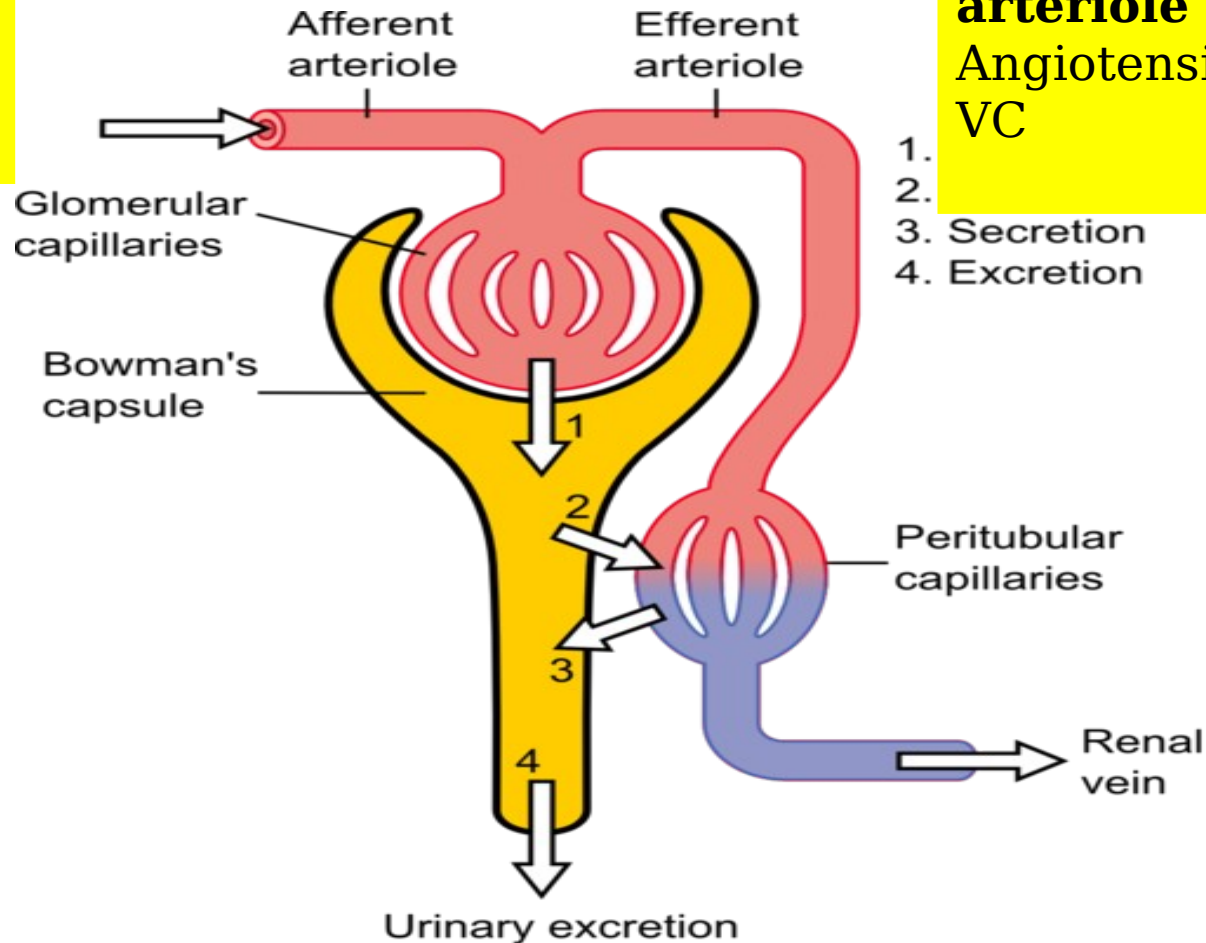
1. Identify the site of action of diuretics
2. Identify different members of diuretics
3. Explain the mechanism of action and adverse effects of different diuretics



# DIURETICS

**Afferent arteriole**  
**PG** → **VD**

**Efferent arteriole**  
**Angiotensin II** → **VC**

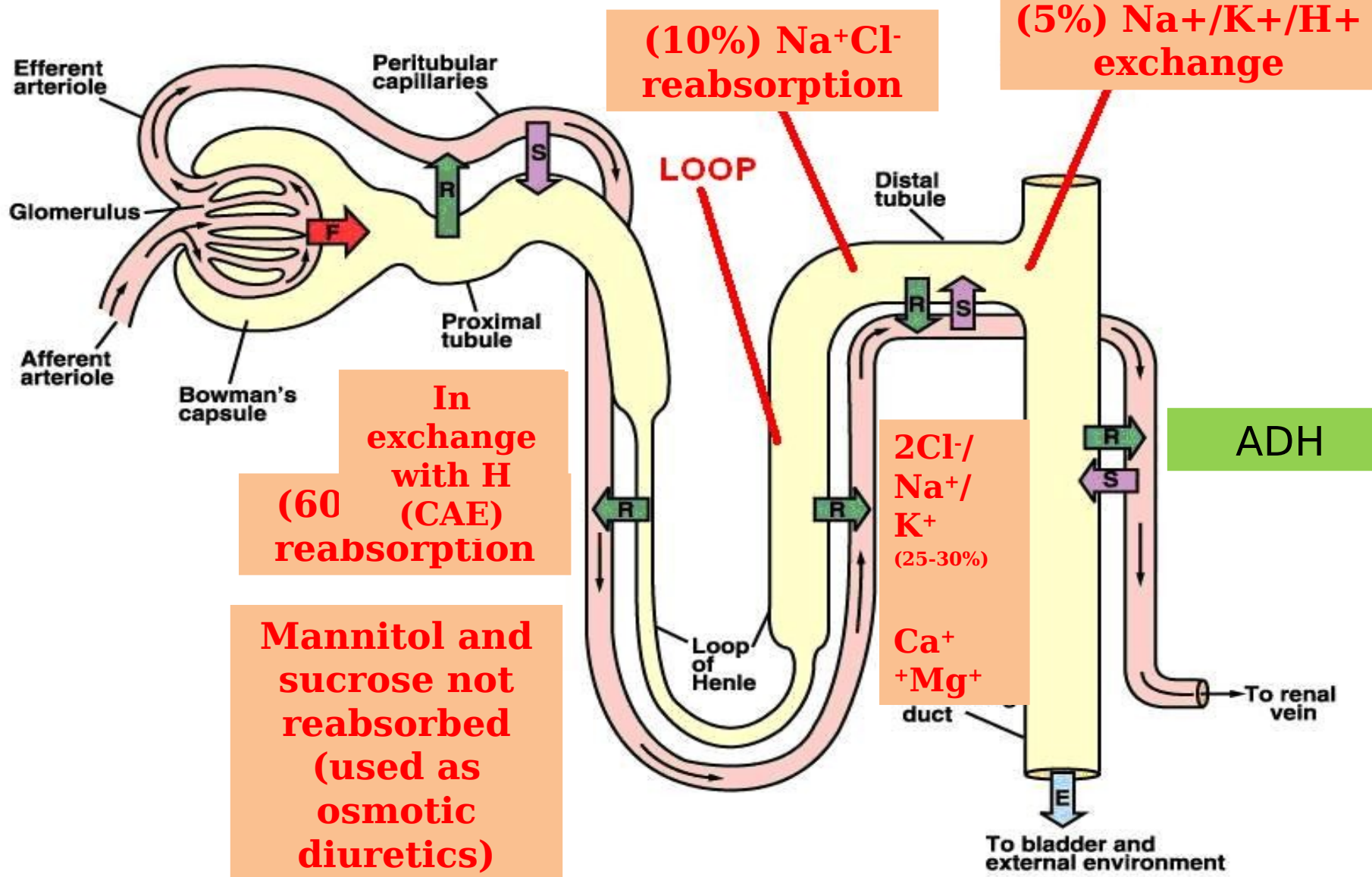


## **Maintenance of Glomerular Filtration in Hypoperfusion States**

In renal hypoperfusion, glomerular pressure is  $\uparrow$  to maintain GFR through:  $\uparrow$  Ag II  $\rightarrow$  VC of efferent arteriole &  $\uparrow$  PG  $\rightarrow$  VD of afferent arteriole  $\rightarrow$   $\uparrow$  blood flow

- In **renal hypoperfusion** states (hypovolemia, diuretic therapy, heart failure), administration of **ACEIs** (→ inhibit efferent VC) or administration of the PG synthesis inhibitors **NSAIDs** (→ inhibit afferent VD) causes marked reduction in glomerular filtration → acute renal failure.

# Transport of water and electrolytes through the nephron



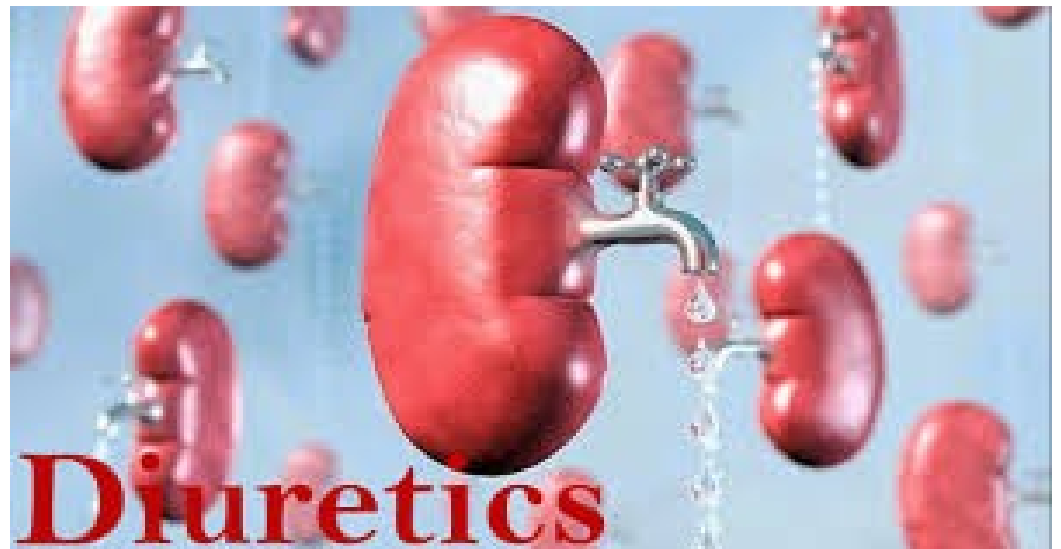
## Medullary hypertonicity:

is created by active reabsorption of  $\text{Na}^+$  coupled with passive transport of urea at this segment. It provides osmotic driving forces for water reabsorption from collecting tubules under the effect of ADH to conserve body water & concentrate urine.

Renal PG interfere with medullary hypertonicity by inhibiting  $\text{Na}$  reabsorption leading to diuresis

# Diuretics

Diuretics are drugs that cause a net loss of sodium and water from the body through the kidney resulting in contraction of the extracellular fluid.

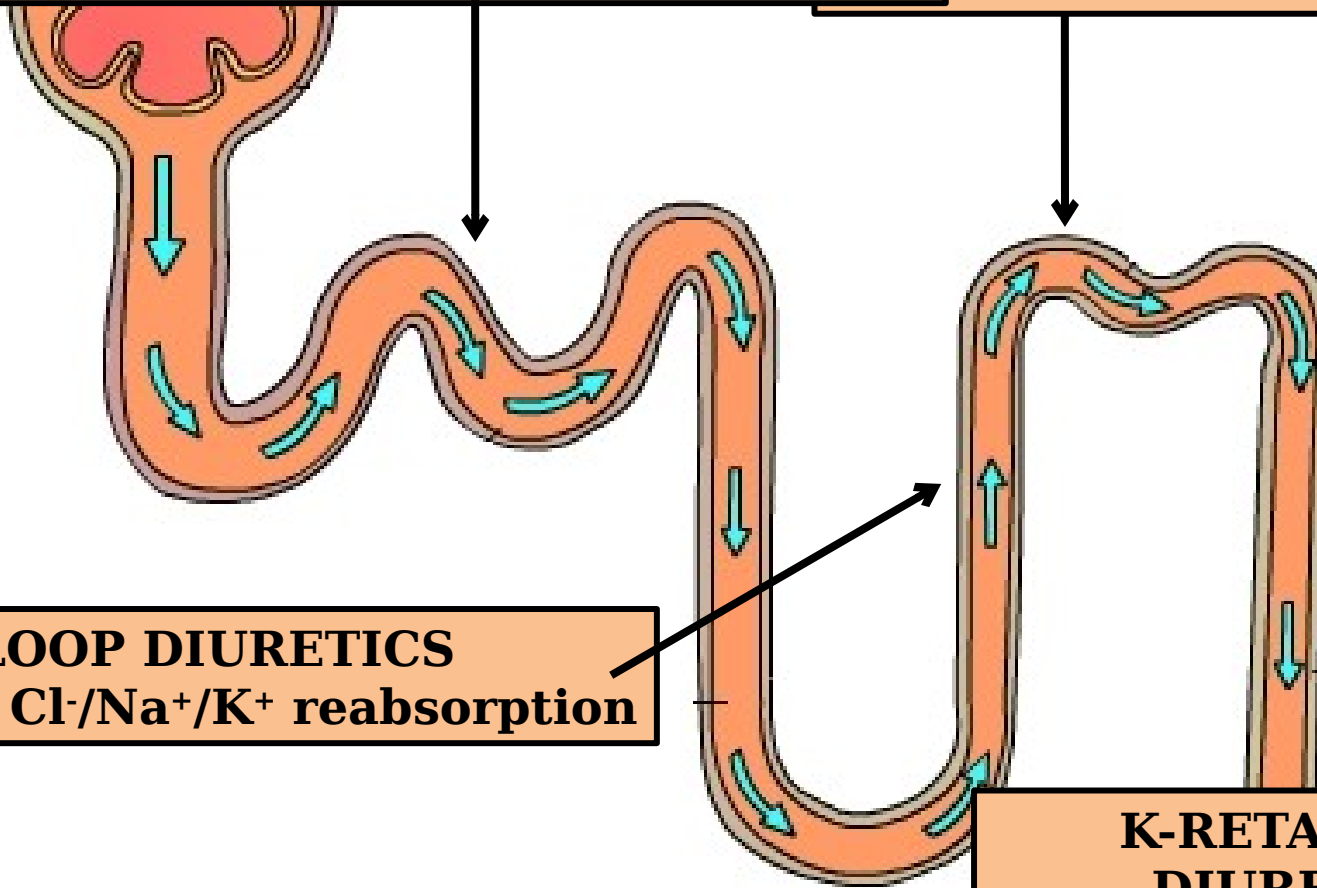


**Osmotic diuretics**  
**Mannitol**

# DIURETICS

**Carbonic anhydrase inhibitors**  
**inhibition of  $\text{NaHCO}_3$  reabsorption**

**THIAZIDE DIURETICS**  
**inhibit active  $\text{NaCl}$  reabsorption**



**LOOP DIURETICS**  
**Block 2  $\text{Cl}^-/\text{Na}^+/\text{K}^+$  reabsorption**

**K-RETAINING DIURETICS**  
**Inhibit  $\text{Na}^+$  reabsorption**  
 **$\text{K}^+$  &  $\text{H}^+$  excretion**

<b>Diuretic</b>	<b>Site of action</b>
<ul style="list-style-type: none"> <li>• Carbonic anhydrase Inhibitors</li> </ul>	Proximal tubule
<ul style="list-style-type: none"> <li>• Osmotic diuretics</li> </ul>	Proximal tubule & loop of Henle
<ul style="list-style-type: none"> <li>• Loop diuretics</li> </ul>	Loop of Henle
<ul style="list-style-type: none"> <li>• Thiazides</li> </ul>	Early Distal tubule
<ul style="list-style-type: none"> <li>• Amiloride</li> <li>• Triamterene</li> <li>• Spironolactone</li> </ul>	Distal tubule and collecting duct

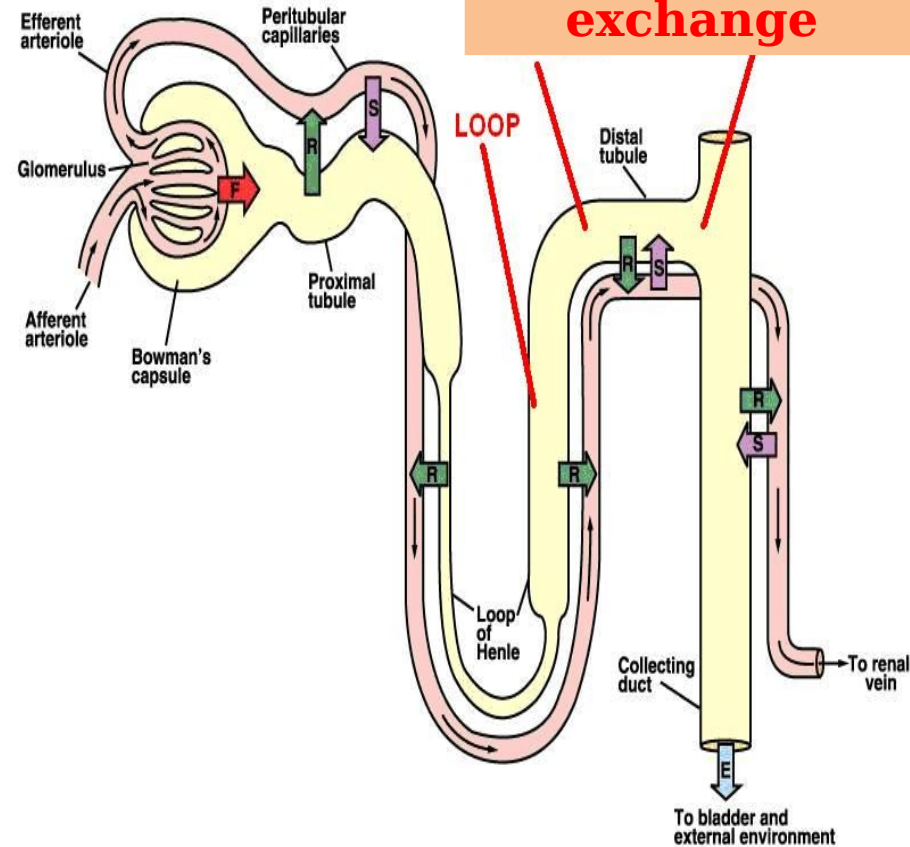
# General principles in diuretic therapy

Aldosterone

**Na<sup>+</sup>/K<sup>+</sup>/H<sup>+</sup> exchange**

Diuretics interfering with reabsorption of Na<sup>+</sup> at earlier (more proximal) sites lead to enhanced Na<sup>+</sup> reabsorption in exchange with K<sup>+</sup> & H<sup>+</sup> at distal tubule (aldosterone-dependent Na<sup>+</sup>/K<sup>+</sup>/H<sup>+</sup> exchange site)

→ hypokalemia and alkalosis.



# Diuretics



## **A. $K^+$ -losing diuretics**

- Loop diuretics.
- Thiazides.
- Osmotic diuretics.
- Carbonic anhydrase inhibitors.

## **B. $K^+$ -sparing diuretics**

- Spironolactone
- Amiloride
- triamterene.

# General principles in diuretic therapy

Diuretics act by different mechanisms and at different sites along the nephron. Thus, they have a synergistic effect if they are combined.



# General principles in diuretic therapy

All diuretics (except spironolactone) have to reach their site of action in the lumen of the nephron, by organic acid or organic base secretory systems .

Therefore, any defect in delivery of diuretics to their sites of action (e.g. in renal impairment) will result in diminished diuretic response.

Diuretic	Route of access to site of action
<ul style="list-style-type: none"> <li>• Carbonic anhydrase Inhibitors</li> </ul>	Organic acid secretion
<ul style="list-style-type: none"> <li>• Osmotic diuretics</li> </ul>	Glomerular filtration
<ul style="list-style-type: none"> <li>• Loop diuretics</li> </ul>	Organic acid secretion
<ul style="list-style-type: none"> <li>• Thiazides</li> </ul>	Organic acid secretion
<ul style="list-style-type: none"> <li>• Amiloride</li> </ul>	Organic base secretion
<ul style="list-style-type: none"> <li>• Triamterene</li> </ul>	Organic base secretion
<ul style="list-style-type: none"> <li>• Spironolactone</li> </ul>	Peritubular circulation

# Lecture quiz

- Which of the following diuretics is associated with hyperkalemia?
- A. Thiazides
  - B. Loop diuretics
  - C. Osmotic diuretics
  - D. Carbonic anhydrase inhibitors
  - E. Spironolactone

# **SUGGESTED TEXTBOOKS**



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7<sup>th</sup> edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14<sup>th</sup> edition) New York: McGraw-Hill Medical.



**Thank You**